

Experiment Number: K12005
Route: Intravenous, Oral Gavage
Species/Strain: Rat/Harlan Sprague-Dawley

Toxicokinetics Data Summary
Compound & Analyte: Octrizole
CAS Number: 3147-75-9

Request Date: 3/12/2021
Request Time: 2:30:16
Lab: BAT

Male

Treatment Group (mg/kg)

2.25 IV^a Blood

30 Gav^b Blood

300 Gav^b Blood

C ₀ min_pred (ng/mL)	20600 ± 7800		
C _{max} _pred (ng/mL)		561 ± 170	3590 ± 850
T _{max} _pred (hour)		3.71 ± 1.08	2.80 ± 0.64
C _{max} _obs (ng/mL)	16500	934	3540
T _{max} _obs (hour)		2.00	2.00
Alpha_Half-life (hour)	0.0552 ± 0.0147	2.98 ± 4.27	2.18 ± 3.63
Beta_Half-life (hour)	0.988 ± 0.190	56.8 ± 233	21.4 ± 18.2
Gamma_Half-life (hour)	15.4 ± 2.4		
k ₀₁ (hour ⁻¹)		0.312 ± 0.560	0.407 ± 0.769
k ₀₁ _Half-life (hour)		2.22 ± 3.99	1.71 ± 3.22
k ₁₀ (hour ⁻¹)	5.88 ± 1.72	0.221 ± 0.323	0.288 ± 0.468
k ₁₀ _Half-life (hour)	0.118 ± 0.035	3.13 ± 4.56	2.41 ± 3.92
k ₁₂ (hour ⁻¹)	5.34 ± 1.83	0.0103 ± 0.0191	0.0269 ± 0.0607
k ₂₁ (hour ⁻¹)	1.33 ± 0.34	0.0128 ± 0.0518	0.0358 ± 0.0327
k ₁₃ (hour ⁻¹)	0.706 ± 0.225		
k ₃₁ (hour ⁻¹)	0.0507 ± 0.0086		
Cl ₁ (mL/hr/kg)	641 ± 81		
Cl ₂ (mL/hr/kg)	582 ± 208		
Cl ₃ (mL/hr/kg)	77.0 ± 24.7		
Cl ₁ _F (mL/hr/kg)		5020 ± 1590	10000 ± 2300
Cl ₂ _F (mL/hr/kg)		233 ± 411	937 ± 798
V ₁ (mL/kg)	109 ± 41		
V ₂ (mL/kg)	437 ± 126		
V ₃ (mL/kg)	1520 ± 450		
V ₁ _F (mL/kg)		22700 ± 37500	34800 ± 62000
V ₂ _F (mL/kg)		18200 ± 103000	26200 ± 16300

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MRT (hour)	3.22 ± 0.55		
AUC _{0-T} (ng/mL·hr)	3690	3840	20100
AUC _{inf} (ng/mL·hr)	3510 ± 440	5980 ± 1950	30000 ± 7400

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LEGEND

MODELING METHOD & BEST FIT MODEL

^a WinNonlin three-compartment model with bolus input, first order output, and $1/Y_{\text{hat}}^2$ weighting (model #18); Cmax_pred based on the model prediction at 0 minutes.

^b WinNonlin two-compartment model with first order input, first order output, and $1/Y_{\text{hat}}^2$ weighting (model #13).

ANALYTE

Octrizole

TK PARAMETERS

C_0min_pred = Fitted plasma concentration at time zero (IV only)
Cmax_obs = Observed maximum plasma concentration
Cmax_pred = Predicted maximum plasma concentration
Tmax_obs = Time at which observed Cmax occurs
Tmax_pred = Time at which predicted Cmax occurs
Alpha_Half-life = Half-life for the alpha phase
Beta_Half-life = Half-life for the beta phase
Gamma Half-life = Half-life for the gamma phase
k01 = Absorption rate constant, ka
k01_Half-life = Half-life of the absorption process to the central compartment
k10 = Elimination rate constant from the central compartment also ke or kelim
k10_Half-life = Half-life for the elimination process from the central compartment
k12 = Distribution rate constant from first to second compartment
k21 = Distribution rate constant from second to first compartment
k13 = Distribution rate constant from first to third compartment
k31 = Distribution rate constant from third to first compartment

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TK PARAMETERS (cont'd)

Cl1 = Clearance of central compartment

Cl2 = Clearance of the secondary compartment

Cl3 = Clearance of the tertiary compartment

Cl1_F = Apparent clearance of the central compartment, also Cl_F for gavage groups in non-compartmental model

Cl2_F = Apparent clearance of the secondary compartment

V1 = Volume of distribution of the central compartment, includes Vd and V volume of distribution

V2 = Volume of distribution for the peripheral compartment

V3 = Volume of distribution for the peripheral compartment

V1_F = Apparent volume of distribution for the central compartment includes Vd_F, V_F for oral groups, and Vc_F

V2_F = Apparent volume of distribution for the peripheral compartment

MRT = Mean residence time

AUC_0-T = Area under the plasma concentration versus time curve, AUC, from time ti (initial) to tf (final), AUClast

AUC_inf = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

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TK PARAMETERS PROTOCOL

BLOOD

IV 2.25 Rat Male

Harlan Sprague Dawley male rats were intravenously administered a single 2.25 mg/kg dose of Octrizole. An automated blood sampling system (Culex) was used for this study. Whole blood samples were taken from n=3 animals/timepoint/per group at pre-dose and 16 timepoints at 0.0333, 0.0833, 0.167, 0.25, 0.333, 0.5, 0.75, 1, 2, 4, 8, 12, 18, 24, 48, and 72 hrs. Parent (free) was analyzed by LC-MS/MS with a lower limit of quantitation (LLOQ) of 5.0 ng/mL. Parameter estimates are reported to three significant figures with standard error (SE). Observed values do not have a reported SE.

BLOOD

Gavage 30 Rat Male, 300 Rat Male

Harlan Sprague Dawley male rats were administered a single gavage dose of 30 or 300 mg/kg Octrizole. An automated blood sampling system (Culex) was used for this study. Whole blood samples were taken from n=3 animals/timepoint/per group at pre-dose and 16 timepoints at 0.0333, 0.0833, 0.167, 0.25, 0.333, 0.5, 0.75, 1, 2, 4, 8, 12, 18, 24, 48, and 72 hrs. Parent (free) was analyzed by LC-MS/MS with a lower limit of quantitation (LLOQ) of 5.0 ng/mL. Parameter estimates are reported to three significant figures with standard error (SE). Observed values do not have a reported SE.